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Docket No: 4280/1M321US1

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of: Alan J. KORMAN et al.

Serial No.: 09/644,668

Art Unit: 1644

Confirmation No.: 5400

Filed: August 24, 2000

Examiner: Jessica H. ROARK

For: HUMAN CTLA-4 ANTIBODIES AND THEIR USES

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**TRANSMITTAL OF INFORMATION DISCLOSURE  
STATEMENT REFERENCES (COURTESY COPY)**

Hon. Commissioner of Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

SIR:

Pursuant to the request of Examiner Jessica H. Roark, Applicants submit herewith courtesy copies of references 1-40 that were originally submitted with Applicants' Information Disclosure Statement ("IDS") mailed on September 25, 2001 for this application. For the Examiner's convenience, Applicants also submit herewith: (1) a copy of Form PTO/SB/08A (Substitute for Form 1449A/PTO), which was submitted as part of the IDS, attached hereto at Exhibit Tab A; and (2) a copy of the return receipt postcard.

Serial No. 09/644,668

Preliminary Amendment and Response to Restriction Requirement

Docket No. 4280/1M321US1

Page 1

## REMARKS

At the outset, Applicants thank Examiner Jessica A. Roark for the courtesies extended during the telephone call to Applicants' undersigned representative on June 2, 2003. During that telephone call, Examiner Roark stated that the references originally submitted with the Information Disclosure Statement (IDS) for this application had been lost by the Patent and Trademark Office (PTO). Examiner Roark indicated that it would help expedite prosecution of the application if Applicants provide courtesy copies of at least the non-patent references.

Pursuant to the Examiner's request and to facilitate the examination of this application, Applicants submit herewith copies the 82 reference documents that were cited in Applicants' IDS. For the Examiner's convenience, a copy of Form PTO/SB/08A (Substitute for Form 1449A/PTO), which was submitted as part of the IDS, is also submitted here at Exhibit Tab A. Applicants note that the references submitted here have been labeled with numbered Exhibit Tabs corresponding to the citations number for each reference on accompanying Form PTO/SB/08A.

Also submit herewith, at Exhibit Tab B, is a true copy of the return receipt postcard which, on information and belief, was submitted with the IDS on September 25, 2001. The postcard has been stamped by the PTO Receiving Office indicating that the documents listed therein (including 82 IDS references) were received by the PTO in their entirety on or about October 1, 2001.

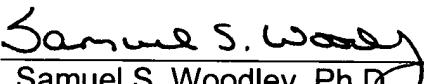
Because this resubmission of those reference documents is due to a PTO error, no fee should be charged for this submission. Nevertheless, should the PTO determine Serial No. 09/644,668 Docket No. 4280/1M321US1  
Preliminary Amendment and Response to Restriction Requirement Page 2

that any fee is required for this submission or that any refund is due for this application. the Commissioner is hereby authorized and requested to charge any required fee(s) and/or credit any refund(s) due to our Deposit Account No. 04-0100.

The Examiner is invited to contact Applicants' undersigned representative again if there is any problem with the receipt of these references or if she believes that it may advance prosecution of this application. An early and favorable examination of this application on the merits is earnestly sought.

Respectfully submitted,

Dated: June 3, 2003

  
\_\_\_\_\_  
Samuel S. Woodley, Ph.D.  
(Reg. No. 43,287)  
Agent for Applicants

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Substitute for form 1449A/PTO

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Application Number	09/644,668
Filing Date	August 24, 2000
First Named Inventor	Korman, Alan J.
Group Art Unit	1632
Examiner Name	Unassigned

Sheet 1 of 5 Attorney Docket Number 014643-010510US

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FAX NO.: 202-415-6000**U.S. PATENT DOCUMENTS**

Examiner Initials *	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
1	6,162,963			Kucherlapati et al.	12-19-2000	
2	6,150,584			Kucherlapati et al.	11-21-2000	
3	6,114,598			Kucherlapati et al.	09-05-2000	
4	6,075,181			Kucherlapati et al.	06-13-2000	
5	6,051,227			Allison et al.	04-18-2000	
6	5,977,318			Linsley et al.	11-02-1999	
7	5,968,510			Linsley et al.	10-19-1999	
8	5,939,598			Kucherlapati et al.	11-17-1999	
9	5,885,796			Lonberg et al.	03-23-1999	
10	5,877,397			Lonberg et al.	03-02-1999	
11	5,874,299			Lonberg et al.	02-23-1999	
12	5,855,887			Allison et al.	01-05-1999	
13	5,844,095			Linsley et al.	12-01-1998	
14	5,814,318			Lonberg et al.	09-29-1998	
15	5,811,097			Allison et al.	09-22-1998	
16	5,789,650			Lonberg et al.	08-04-1998	
17	5,770,429			Lonberg et al.	06-23-1998	
18	5,770,197			Linsley et al.	06-23-1998	
19	5,661,016			Lonberg et al.	08-26-1997	
20	5,633,425			Lonberg et al.	05-27-1997	
21	5,625,126			Lonberg et al.	04-29-1997	
22	5,569,825			Lonberg et al.	10-29-1996	
23	5,545,806			Lonberg et al.	08-13-1996	

**FOREIGN PATENT DOCUMENTS**

Examiner Initials *	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
24	PCT	WO00/37504			Hanson et al.	06-29-2000		
25	PCT	WO00/10383			Tomizuka et al.	03-02-2000		abstract only
26	PCT	WO98/42752			Kuchroo et al.	10-01-1998		

Examiner Signature	Date Considered
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**EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST-3). <sup>4</sup> Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST-16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

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Substitute for form 1449A/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> <i>(use as many sheets as necessary)</i>			<b>Complete If Known</b>	
			Application Number	09/644,668
			Filing Date	August 24, 2000
			First Named Inventor	Korman, Alan J.
			Group Art Unit	1632
			Examiner Name	Unassigned
Sheet	2	of	5	Attorney Docket Number
			014643-010510US	

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Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
27	PCT	WO98/37757			Tomizuka et al.	09-03-1998		abstract only
28	PCT	WO98/24893	A2		Jakobovits et al.	06-11-1998		
29	PCT	WO98/24893	A3		Jakobovits et al.	06-11-1998		
30	PCT	WO98/24884			Lonberg et al.	06-11-1998		
31	PCT	WO97/07671			Tomizuka et al.	03-06-1997		abstract only
32	PCT	WO96/34096			Kucherlapati et al.	10-31-1996		
33	PCT	WO96/33735			Kucherlapati et al.	10-31-1996		
34	PCT	WO95/33770			Gribben et al.	12-14-1995		
35	PCT	WO94/25585			Lonberg et al.	11-10-1994		
36	PCT	WO94/02602			Kucherlapati et al.	02-03-1994		
37	PCT	WO93/12227			Lonberg et al.	06-24-1993		
38	PCT	WO92/22645			Huang et al.	12-23-1992		
39	PCT	WO92/03918			Lonberg et al.	03-19-1992		
40	PCT	WO91/10741			Kucherlapati et al.	07-25-91		

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Sheet

3 of 5

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Application Number	09/644,668
Filing Date	August 24, 2000
First Named Inventor	Korman, Alan J.
Group Art Unit	1632
Examiner Name	Unassigned
Attorney Docket Number	0146432-010510US

### OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	41	BLAIR et al. "Cutting edge: CTLA-4 ligation delivers a unique signal to resting human CD4 T cells that inhibits interleukin-2 secretion but allows Bcl-X <sub>L</sub> induction," The J. of Immunology 22:1767 (1998)	
	42	BLUESTONE (1997) J. Immunol. 158:1989-1993	
	43	BRUNET et al., Immunol. Rev. 103:21-36 (1988)	
	44	BRUNET et al., Nature 328:267-270(1987)	
	45	CHAMBERS (1997) Curr. Opin. Immunol. 9:396-404	
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	47	CLARK (1986) Human Immunol. 16:100-113	DPL.CX
	48	DAMLE et al., Proc. Natl. Acad. Sci. 78:5096-6001 (1981)	
	49	DARIAVACH et al., Eur. J. Immunol. 18:1901-1905 (1988)	
	50	ELSAS et al. "Combination immunotherapy of B16 melanoma using anti-cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) and granulocyte/macrophage colony-stimulating factor (GM-CSF)-producing vaccines induces rejection of subcutaneous and metastatic tumors accompanied by autoimmune depigmentation," J. Exp. Med. 190:355-366 (1999)	
	51	FISHWILD et al. "High-avidity human IgGk monoclonal antibodies from a novel strain of minilocus mice," Nature Biotechnology 14:845-851 (1996)	
	52	FREEDMAN (1987) J. Immunol. 138:3260-3267	
	53	FREEMAN (1989) J. Immunol. 143:2714-2722	
	54	GRIBBEN et al. "CTLA4 mediates antigen-specific apoptosis of human T cells," Proc. Natl. Acad. Sci. USA 92:811-815 (1995)	
	55	HURWITZ et al. "CTLA-4 blockade synergizes with tumor-derived granulocyte-macrophage colony-stimulating factor for treatment of an experimental mammary carcinoma," Proc. Natl. Acad. Sci. USA 95:10067-10071 (1998)	

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Substitute for form 1449A/PTO		<i>Complete If Known</i>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> <i>(use as many sheets as necessary)</i>		Application Number	09/644,668
		Filing Date	August 24, 2000
		First Named Inventor	Korman, Alan J.
		Group Art Unit	1632
		Examiner Name	Unassigned
Sheet	4	of	5
		Attorney Docket Number	0146432-010510US

**OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS**

56	HURWITZ et al. "Immunotherapy of primary prostate cancer in a transgenic model using a combination of CTLA-4 blockade and tumor cell vaccine," Cancer Research 60:2444-2448 (2000)	<i>DRA/CT/3</i>
57	KEARNEY (1995) J. Immunol. 155:1032-1036	
58	KOHNO et al., Cell. Immunol. 131:1-10 (1990)	
59	KRUMMEL et al. "CD28 and CTLA-4 have opposing effects on the response of T cells to stimulation," (1995) J. Exp. Med. 182:459-465	
60	KRUMMEL et al. "CTLA-4 engagement inhibits IL-2 accumulation and cell cycle progression upon activation of resting T cells," J. Exp. Med 183:2533-2540 (1996)	
61	KRUMMEL et al. "Superantigen responses and co-stimulation: CD28 and CTLA-4 have opposing effects on T cell expansion in vitro and in vivo," (1996) Int'l Immunol. 8:519-523	
62	KWON et al. "Manipulation of T cell costimulatory and inhibitory signals for immunotherapy of prostate cancer," proc. Natl. Acad. Sci. USA 94:8099-8103 (1997)	
63	Lafage-Pochitaloff et al., Immunogenetics 31:198-201 (1990)	
64	LEACH et al. "Enhancement of antitumor immunity by CTLA-4 blockade," Science. 271:1734-1736 (1996)	
65	LESSLAUER et al., Eur. J. Immunol. 16:1289-1296 (1986)	
66	LINDSTEN et al., Science 244:339-343 (1989)	
67	LINSLEY et al. "Coexpression and functional cooperation of CTLA-4 and CD28 on activated T lymphocytes," J Exp. Med. 176:1595-1604 (1992)	
68	LINSLEY et al. "CTLA-4 is a second receptor for the B cell activation antigen B7," J. Exp. Med. 174:561-569 (1991)	
69	LINSLEY et al., J. Exp. Med. 173:721-730 (1991)	
70	LINSLEY et al., Proc. Natl. Acad. Sci. USA 87:5031-5035 (1990)	
71	LONBERG et al. "Human antibodies from transgenic mice," International Review of Immunology. 13:65-93 (1995)	
72	LUHDER (1998) J Exp. Med. 187:427-432	

Examiner Signature	Date Considered
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<sup>1</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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Sheet

5 of 5

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Application Number	09/644,668
Filing Date	August 24, 2000
First Named Inventor	Korman, Alan J.
Group Art Unit	1632
Examiner Name	Unassigned

Attorney Docket Number 0146432-010510US

### OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

73	MATSUI (1999) J. Immunol. 162:4328-4335
74	MCCOY et al. "Protective immunity to nematode infection is induced by CTLA-4 blockade," J. Exp. Med 186:183-187 (1997)
75	NEUBERGER "Generating high-avidity human Mabs in mice," Nature Biotechnology 14:826 (1996)
76	THOMPSON (1997) Immunity 7:445-450
77	THOMPSON et al., Proc. Natl. Acad. Sci 86:1333-1337 (1989)
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79	WALUNAS, et al., "CTLA-4 can function as a negative regulator of T Cell activation," Immunity. 1:405-413 (1994)
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81	YANG et al. "Eradication of established tumors by a fully human monoclonal antibody to the epidermal growth factor receptor without concomitant chemotherapy," Cancer Research 59:1236-1243 (1999)
82	YOKOCHI (1981) J. Immunol. 128:823

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Examiner Signature	Date Considered
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